THE EFFECTS OF AMIKACIN ON AUTONOMIC AND NEUROMUSCULAR TRANSMISSION

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Aminoglycoside antibiotics induce prolonged muscle paralysis in anaesthetic practice when used in combination with some muscle relaxants and general anaesthetics (see Pittinger & Adamson, 1972).

The effects of amikacin, a new aminoglycoside antibiotic, have been tested on neuromuscular and autonomic transmission in the isolated mouse phrenic nerve-hemidiaphragm and chick biventer cervicis muscle preparations, in the anaesthetized cat, and by intracellular recording techniques in the isolated rat phrenic nerve-hemidiaphragm preparation.

In the mouse hemidiaphragm amikacin was five times less active than neomycin in depressing indirectly elicited twitches. The neuromuscular block induced by amikacin or neomycin was completely reversed by doubling the calcium concentration of the bathing solution, and was only partially reversed by neostigmine (1 µg/ml; 3.0×10^{-6} M). The spectrum of reversibility was similar to that seen after neuromuscular block produced by magnesium ions. The similarity of the action of amikacin to magnesium was also illustrated in the rat hemidiaphragm in which amikacin (2.5 mg/ml; 4.27mM) reduced endplate potential amplitude below the threshold required to elicit muscle twitching. The endplate potential amplitudes fluctuated randomly and several failures were observed. Miniature endplate potentials were of normal amplitude indicating that postjunctional sensitivity remained intact. However, in the chick biventer cervicis muscle amikacin (2.5 mg/ml; 4.27 mM) reduced responses to both nerve stimulation and to added agonists indicating a component of postjunctional activity. Magnesium ions produced similar effects.

In the anaesthetized cat large doses of amikacin (160-200 mg/kg) were required to block neuromuscular transmission. At these and lower dose levels ganglionic transmission was also impaired with a resultant fall in blood pressure and in heart rate. Smaller doses of amikacin (10-20 mg/kg) were effective in increasing the neuromuscular block produced by tubocurarine.

Thus, we conclude that amikacin depresses cholinergic transmission both at ganglia and at the neuromuscular junction. Most of the evidence points to a prejunctional magnesium-like depression of acetylcholine release, but a component of postjunctional activity has also been demonstrated.

Pittinger, C. & Adamson, R. (1972). An. Rev. Pharmac., 12, 169-184.

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